

REMARKS

This Amendment, filed in reply to the Office Action dated February 27, 2009, is believed to be fully responsive to each point of objection and rejection raised therein. Accordingly, favorable reconsideration on the merits is respectfully requested.

Claims 1-10 are rejected. Claims 1 and 8 are amended herewith to recite that the liquid medium contains "2% mass or more of soybean powder or defatted soybean powder." Support for this recitation can be found throughout the specification as originally filed, and at, for example, page 10, lines 12-14.

No new matter is added by way of this amendment. Entry and consideration of this amendment are respectfully requested.

Withdrawn Rejections

Applicants thank the Examiner for expressly indicating that the rejection of Claims 1-10 under 35 U.S.C. § 102(b), over Ohno #1, is withdrawn in view of Applicants' arguments.

Further, Applicants understand the current Office Action to be an accurate and complete representation of all outstanding rejections. Accordingly, Applicants understand that *all* the previous rejections of record have been vacated, in view of the fact that no rejections of record are either reiterated, or indicated as being maintained, in the outstanding Office Action.

Claims 6 and 7 are Enabled Under 35 U.S.C. § 112, first paragraph

On page 3 of the Office Action, the Examiner rejects Claims 6 and 7 under 35 U.S.C. § 112, first paragraph, as lacking enablement.

In making the rejection, the Examiner appears to assert that the methods of Claims 6 and 7 require a specific strain of *Bacillus subtilis*, and that in the absence of adequate guidance as to how to reproduce such a strain (*i.e.*, without undue experimentation), a deposit is required, unless the strain was known and publicly available. The Examiner acknowledges that a deposit of the strain recited in Claims 6 and 7 (*i.e.*, *Bacillus subtilis* SD142) has been made by Applicants, but asserts that such is insufficient in itself to support enablement. Rather, the Examiner asserts that a Statement of Availability pertaining to the deposit (*i.e.*, FERM BP-08427) is required.

Solely to advance prosecution of the Application, and without acquiescing to the merits of the rejection, Applicants submit herewith a Statement of Availability pertaining to *B. subtilis* strain SD142. Applicants respectfully submit that such obviates the rejection.

Withdrawal of the rejection is respectfully requested.

Claims 1-10 are Patentable Under 35 U.S.C. § 103

1. On page 4 of the Office Action, Claims 1-9 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Phae *et al.*, of record, in view of Tulin *et al.* (*Biotechnology and Bioengineering*, 1992, 40:844-850), DeMain *et al.* (*J. Bacteriol.*, 1958, 75(5):517-522) and Gary *et al.* (*J. Bacteriol.*, 1952, 64(4):501-512).

In making the rejection, the Examiner contends that Phae *et al.* disclose liquid fermentation of *B. subtilis* NB22 in a medium containing polypepton, glucose and KH_2PO_4 , citing the Materials and Methods section. The Examiner contends that the polypepton concentration may be 50 g/L, which the Examiner equates to be 5%. The Examiner appears to take the position that, in view of Tulin *et al.*, one of ordinary skill in the art would reasonably construe polypepton as being an extract of soybean powder, as claimed. Regarding the subject

matter of Claim 4, although the Examiner acknowledges that Phae *et al.* only disclose the addition of KH_2PO_4 , the Examiner contends that it was well-known in the art that both K_2HPO_4 and KH_2PO_4 are nutrients for *B. subtilis*, and that such is evidenced by Gary *et al.*, citing page 501, and DeMain *et al.*, citing page 517, column 2. The Examiner contends that one of ordinary skill in the art would readily have substituted one for the other, because the art allegedly recognized both compounds as being used for the same purpose.

Regarding Claims 6 and 7, the Examiner acknowledges that Phae *et al.* do not disclose *B. subtilis* SD142, or a mutant thereof. However, the Examiner maintains his position that because such strains are both of the species *B. subtilis*, and both produce iturin A, the strains are assumed to be the same or sufficiently similar as to exhibit the same or similar properties. The Examiner takes much the same position regarding the subject matter of Claim 3, that is, that an absence of surfactin production is presumed to be an inherent characteristic of *B. subtilis* NB22.

Further, the Examiner expressly acknowledges that Phae *et al.* do not disclose production of iturin A to a concentration of 1.5 g/L. However, in an attempt to rectify this deficiency, the Examiner appears to assert that product yield of iturin A was known to be a result-effective variable, and that it would be routine optimization for one of ordinary skill in the art to modify the iturin A yield to that instantly claimed.

Applicants respectfully disagree, and traverse the rejection in view of the following remarks.

Initially, Applicants note that Claims 1 and 8 are amended herewith to recite that the bacteria are cultivated in “a liquid medium containing 2% mass or more of soybean powder or defatted soybean powder.” This recitation is amply supported by the specification as filed, such as at, for example, page 10, lines 12-14. Neither Phae *et al.*, Tulin *et al.*, DeMain *et al.*, nor Gary

et al. disclose a liquid medium containing 2% mass or more of soybean powder or defatted soybean powder, as claimed. Accordingly, neither Phae *et al.*, Tulin *et al.*, DeMain *et al.*, nor Gary *et al.*, taken alone or in combination, teach each and every element of Claims 1 and 8. Claims 2-7, and Claims 9 and 10, are not rendered obvious at least by virtue of their dependency on Claims 1 and 8, respectively.

Applicants respectfully submit that the cited references do not render obvious the subject matter of Claims 1-9 at least for the foregoing reason.

Further, and independent of the above, Applicants disagree that the Examiner has met his burden in establishing a *prima facie* case of obviousness, for the following reasons.

First, on page 7 of the Office Action, it is expressly acknowledged that the method of Phae *et al.* does not result in a yield of iturin A to a level of 1.5g/L or more. However, the Examiner appears to suggest that routine optimization of result-effective variables “such a[s] pH, aeration rate, temperature and reaction time,” would be sufficient to mediate iturin production to a level of 1.5g/L. Applicants strongly, but respectfully, disagree. As was noted in the response to the Office Action mailed November 12, 2007, Phae *et al.* had already undertaken considerable optimization, concluding that “30°C was optimal in the production of iturin.” Further, in Figures 2 and 10, Phae *et al.* monitor iturin A production over time until the concentration of iturin A in the medium reaches a plateau, *i.e.*, optimization of time. Even at the plateau phase, iturin production was still substantially less than 1.5g/L. In other words, Phae *et al.* had already established that optimization of time and temperature was wholly insufficient to produce iturin levels even approaching 1.5g/L. Accordingly, one of ordinary skill in the art, having read Phae *et al.*, would not have possessed any motivation to optimize these conditions, as such had already been performed by Phae *et al.*, nor would they have possessed any expectation of success in

increasing iturin production by optimization of such variables, because Phae *et al.* demonstrate such to be insufficient.

Furthermore, while Claims 3, 6 and 7 are not rendered obvious at least by virtue of their dependency on Claim 1 as amended, Applicants respectfully disagree with the Examiner's reasoning that because the NB22 and SD142 bacterial strains are both of the species *B. subtilis*, and both produce iturin A, they are presumed to be the same strain and that an absence of surfactin production is thus an inherent characteristic of *B. subtilis* NB22. In contradistinction to *B. subtilis* SD142, *B. subtilis* NB22 does not produce 50ppm or less surfactin in the culture medium during cultivation. While data in this regard is not required to obviate the rejection in view of the foregoing reasons, to clarify the record, Applicants will submit a supplemental Declaration under 37 C.F.R. § 1.132 in due course, providing experimental data establishing such.

Withdrawal of the rejection is respectfully requested.

2. On page 7 of the Office Action, Claims 1-10 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Phae *et al.*, of record, in view of Tulin *et al.* (*Biotechnology and Bioengineering*, 1992, 40:844-850), DeMain *et al.* (*J. Bacteriol.*, 1958, 75(5):517-522) and Gary *et al.* (*J. Bacteriol.*, 1952, 64(4):501-512), as applied above, and further in view of Ohno #1, of record.

In making the rejection, the Examiner states that Claims 1-9 are rejected for *the same reasons* as discussed in the obviousness rejection set forth above.

Contrariwise, however, the Examiner proceeds to rely upon Ohno #1 to disclose the production of iturin to a concentration of “6g/mL or 6000 g/L.”¹ Further, the Examiner cites to Figure 7 of Ohno #1 to assert that Ohno #1 disclose that high yields of iturin can be achieved by increasing moisture in the substrate (*i.e.*, the okara). Notably, and contrary to the Examiner’s position in the previous Office Action, the Examiner now acknowledges that Ohno #1 do not teach fermentation in a “liquid” medium. Rather, the Examiner now states that “Ohno #1 uses a solid substrate fermentation method.” (Emphasis added.) However, in an attempt to render obvious the presently claimed invention, the Examiner contends that one of ordinary skill in the art would readily have adapted the method of Ohno #1 to a liquid fermentation by adding more liquid media. Motivation for such is asserted to be found in Ohno #1, who allegedly disclose that high yields of iturin can be achieved with more moisture in their substrate, and in Phae *et al.*, who merely disclose that iturin production by *B. subtilis* NB22 can occur in a liquid medium.

Regarding Claim 10, the Examiner contends that Ohno #1 disclose that solid cultures of *B. subtilis* NB22 can be obtained and placed on fields as a fertilizer, citing page 805, column 2. From this, the Examiner contends that one of ordinary skill in the art would readily have appreciated that solid cultures are “dried[,] or at the very least not a solution so much of the media would need to be removed.”

Applicants respectfully disagree, and traverse the rejection in view of the following remarks.

¹ As noted in the response to the Office Action of June 6, 2008, this calculation is flawed. Using the Examiner’s own calculation yields a value of 6g/L, three orders of magnitude less than that asserted in the rejection.

Initially, Applicants note that Claims 1 and 8 are amended herewith to recite that the bacteria are cultivated in “a liquid medium containing 2% mass or more of soybean powder or defatted soybean powder.” Neither Phae *et al.*, Tulin *et al.*, DeMain *et al.*, Gary *et al.*, nor Ohno #1 disclose a liquid medium containing 2% mass or more of *soybean powder or defatted soybean powder*, as claimed. Accordingly, neither Phae *et al.*, Tulin *et al.*, DeMain *et al.*, Gary *et al.*, nor Ohno #1, taken alone or in combination, teach each and every element of Claims 1 and 8. Claims 2-7, and Claims 9 and 10, are not rendered obvious at least by virtue of their dependency on Claims 1 and 8, respectively.

Applicants respectfully submit that the cited references do not render obvious the subject matter of Claims 1-10 at least for the foregoing reason.

In addition, and independent of the above, Applicants note that while the Examiner expressly states that Claims 1-9 are rejected for the same reasons as in the rejection above, the rationale employed in each rejection is entirely different. In the instant rejection, the rejection is predicated on the basis that one of ordinary skill in the art would readily have added more liquid medium to the solid-state fermentation of Ohno #1 to arrive at a liquid medium for fermentation.

Nevertheless, while Claims 1-10 are not obvious at least in view of the amendments to Claims 1 and 8 submitted herewith, Applicants respectfully submit that the rationale employed in the rejection is inapt, and as a consequence, a *prima facie* case of obviousness has not been established.

First, as Applicants asserted in the Response filed September 8, 2008, even had the Examiner’s own calculations been executed correctly (which would have provided a value of 6g/L, not 6kg/L), such calculations nevertheless fail to take into consideration the *necessary increase in volume* upon addition of the okara in arriving at a value of 6g/L. For this reason,

Ohno #1 do not produce okara to a level of 6g/L, not even in a solid-state fermentation. Further, Applicants respectfully submit that the Examiner has neglected to consider that upon adapting the solid-state fermentation process of Ohno #1 to liquid fermentation, the concentration of the iturin, in terms of g/L, would drastically decrease due to the significant increase in volume required to make the okara a "liquid medium." Applicants point out that, the reason why the experiments of Ohno #1 were able to produce a relatively high concentration of iturin, in g/L terms, was because it was a solid-state fermentation, with very little liquid present. Applicants, however, claim a method for *liquid fermentation*.

Furthermore, to establish a *prima facie* case of obviousness, it is necessary to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007). In making the rejection, the Examiner appears to suggest that one of ordinary skill in the art would readily have adapted the fermentation method of Ohno #1 (*i.e.* solid-state fermentation on okara) to a liquid fermentation. However, no credible reason is proffered as to why one of ordinary skill in the pertinent art would have made such a modification. To the contrary, Ohno #1 actually teach away from such a modification. On page 805, column 2, Ohno #1 state that "[s]olid-state fermentation for iturin A production is simple to operate, as well as requiring a shorter time (48h) for the completion of production, compared with 120h in liquid fermentation. The concentration of total iturin A produced is 6-8 times higher than that in liquid fermentation, implying that a smaller amount of solvent would be necessary for the purification of iturin A from the fermented product." (Emphasis added.) In view of such a teaching, one of ordinary skill in the art would not have possessed any motivation to modify the solid-state fermentation of Ohno #1 to a liquid fermentation, due to the decrease in

concentration and increased fermentation time. Applicants respectfully submit that the Examiner's position is firmly grounded in impermissible hindsight reconstruction, relying solely upon data gleaned from Applicants' disclosure.

Further, Applicants submit that the Examiner's reliance on Figure 7 to provide motivation for one of ordinary skill in the art to add additional liquid to okara to undertake liquid fermentation is flawed. Figure 7 clearly depicts iturin production during solid-state fermentation, when dehydrated okara is rehydrated with varying amounts of liquid. Notably, on page 801, column 1, Ohno #1 state that non-dehydrated (*i.e.*, natural okara) has a moisture content of 81%. As would be appreciated by those of ordinary skill in the art, the experiments depicted in Figure 7 were performed to identify whether dehydration, and subsequent hydration of okara, had any effect on iturin production. On page 805, column 1, Ohno #1 disclose that "[a] moisture content of 82% was optimal." Further, one of ordinary skill in the art would also understand from Figure 7, particularly the results obtained when using an initial moisture content of 90%, that moisture contents above 82% actually result in a decrease in iturin production. Accordingly, one of ordinary skill in the art would understand that Figure 7 provides a clear demonstration that increasing the moisture content beyond that of natural okara (which is a solid-phase) decreases iturin production. Accordingly, Ohno #1 actively teach away from increasing the moisture content above that of normal okara such that one of ordinary skill in the art would not have possessed any motivation to add additional liquid to the okara of Ohno #1.

In view of the foregoing, Applicants respectfully submit that Claims 1-10 are not rendered obvious in view of the cited references.

Withdrawal of the rejection is respectfully requested.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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